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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/26/2001

Karl-Heinz Drexhage

ARDEN-JACOB

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06/01/2004

HENRY M FEIEREISEN, LLC
350 FIFTH AVENUE
SUITE 4714
NEW YORK, NY 10118

EXAMINER

CERPERLEY, MARY

ART UNIT

PAPER NUMBER

1641

DATE MAILED: 06/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/980,531

Applicant(s)

DREXHAGE ET AL.

Examiner

Mary (Molly) E. Ceperley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on March 01, 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20-36 and 38-49 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 20-36 and 38-49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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1) It is noted that claim 38 has not been properly amended. The full deletion and/or substitution of terms which define Y is incorrect and a period appears in the middle of the claim. See also the second paragraph of page 20 of the March 01, 2004 response.

2) Although specific claims are cited in the rejections below, these rejections are also applicable to all other claims in which the noted problems/language occur.

3) The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4) Claims 20-25 and 44-47 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: steps which define "a procedure for detecting analytes" including steps wherein the analyte contained in a sample is contacted with a labeled receptor and the resulting complex is detected and the detection is correlated with the presence/amount of analyte in a sample. Alternatively, the use of Jepson terminology is suggested to overcome this rejection, for example: "In an immunoassay or nucleic acid hybridization method {specification, page 4, lines 14-18} for the detection of an analyte in a sample, the improvement which comprises using a labeled receptor for the analyte {specification, page 4, lines 8-10} wherein the label is a compound of the formula I...".

5) Claims 20-36 and 38-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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a) It is unclear what is meant by the term "substituents" used in the definition of variables R_9 - R_{12} , i.e. it is unclear what the nature/structure of appropriate "substituents" are (first Office action, paragraph **6)b)**).

b) The rejection of paragraph **6)c)** of the first Office action is maintained for the reasons of record, i.e. exactly what ring structures may be formed is unclear. Claim 20 claim is readable, for example, on compounds which contain multiple heteroatoms such as sulfur and oxygen in ring systems wherein R_9 and R_{10} are joined. It is also unclear which "adjacent substituents" are combined to prepare the ring systems. To overcome this rejection, it is suggested that applicants define the ring structures to be limited to the types described at pages 6-16 of the specification.

c) The claims are again rejected for the reason set forth in paragraph **6)d)** of the first Office action. It is suggested that applicants replace the terminology "at least one of" with the standard Markush terminology, for example, "selected from the group consisting of hydrogen...and cyclic hydrocarbon" which specifies that each of R_9 - R_{12} may independently be any of the listed definitions. The term "at least one of" inconsistently implies the possibility that more than one of each defined variable may be present. See also, claim 30.

d) The claims are again rejected for the reason set forth in paragraph **6)f)** of the first Office action. A "polyether" (which contains oxygen) is conventionally defined as a moiety such as a $-(OCH_2-OCH_2CH_2)_x-$ group (a polyoxyalkylene). A "hydrocarbon group", by definition, consists of only carbon and hydrogen.

e) The claims are again rejected for the reason set forth in paragraph **6)g)** of the first Office action. Applicants' comments regarding this rejection appear to be at odds with the amended language of claim 20. As amended, the definitions of $-N(R_{11})(R_{12})$ and $=N(R_9)(R_{10})$ do not require that "the O-substitution is symmetrical for each of the amino groups". As amended, $-N(R_{11})(R_{12})$ can be $-OR_9$ while $=N(R_9)(R_{10})$ is $=O$. It would appear that a change in the term "at least one of" to "either" would be consistent with "the O-substitution" being symmetrical for each of the amino groups. However, note that structure JF 42, cited by applicants, does not contain an $-OR_9$ moiety.

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f) Claim 20 remains indefinite for the reason stated in paragraph **6)h)** of the first Office action. The amended claim language is still confusing. It would appear that the following language may overcome the noted problem: "wherein **a)** either R₁ is bridged with R₁₀ to form a ring system or R₁ is bridged with R₉ to form a ring system and **b)** either R₂ is bridged with R₉ or R₂ is bridged with R₁₀ to form a ring system". See also, claim 26. Note that in claim 20, as written, the R numbers used to form the various rings of "R₁ bridged with R₁₀ and R₂ with R₉" appear to be in error. For example, it would appear that R₁ would be bridged with R₉ rather than R₁₀.

g) Claim 29 is again rejected for the use of the term "aromatic ring system" which finds no antecedent support in claim 26 (see paragraph **i)** of the first Office action).

h) Claim 31 is again rejected for the reason set forth in paragraph **6)j)** of the first Office action. Applicants' comments in the first paragraph of page 20 of the March 01, 2004 response are noted. However, in claim 26 (from which claim 31 depends) R₁₂ is bridged with R₁₁ **or** R₇ is bridged with R₁₂, which is inconsistent with the structures IVc-IVd of claim 31.

i) Claims 32-36 are again rejected for the reasons set forth in paragraph **k)** of the first Office action. It is unclear how or at what site on the "various substituents" the coupling occurs. The term "further comprising" also indicates that there may be an additional unspecified "coupling" group present on the compound. Exactly what is meant to be encompassed by the claim is unclear.

j) Claim 26 is again rejected for the reason stated in paragraph **6)n)** of the first Office action. The term used in the claim is "4-diaminomethylphenyl and not "4-dimethylamino" as stated in the third paragraph of page 20 of the March 01, 2004 response. Note additionally that a "4-dimethylamino" moiety is not a definition of R₄ in claim 20 i.e. R₄ is defined as unsubstituted aryl.

k) The claims are again rejected for the reasons stated in paragraph **6)e)** of the first Office action. The term "optionally selected from" still appears as a definition of R₉-R₁₂. Additionally, it is unclear what the term "optionally selected from...in the chain" modifies.

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l) For claim 44, the term "hydrocarbon", by definition, cannot include a "heteroaryl" moiety. Similarly, see claim 45 in which the term "hydrocarbon" incorrectly concludes a "heteroatom". See also, claims 46 and 47.

m) Claim 46 is indefinite and confusing. It is unclear to what the term "are from..." refers.

n) For claim 48, a "halogen" is defined as F, Cl, Br or I; this term cannot be defined as "a hydroxyl or thiol group". Further, there is no antecedent basis in claim 38 for the terms "hydroxyl" and "thiol".

o) Claim 49 is indefinite in not specifying at what point and how the "compound" is "covalently coupled to a receptor".

p) The compounds of formulas IVa and IVb of claim 31 are not encompassed by the structure of formula I of independent claim 26. The compound of formula I is required to have at least five rings according to the limitation of the last three lines of claim 26. Applicants' statement at page 22 of the March 01, 2004 that "the compounds as now claimed possess a basic structure of three rings in addition to at least one more ring comprising one of the amino groups" is inconsistent with the recited limitation of claim 26 which requires, at a minimum, five rather than four rings in the basic structure.

6) Claims 20-36 and 44-49 are rejected under 35 USC 112, first paragraph, because the specification, while being enabling for the preparation of some of the compounds of the formula I of claim 20 which contain the groups $-N(R_{11})(R_{12})$ and $=N^+(R_9)(R_{10})$ as described in claim 38, does not reasonably provide enablement for the preparation of compounds of formula I wherein either or both of $-N(R_{11})(R_{12})$ and $=N^+(R_9)(R_{10})$ are replaced by the groups $-OR_9$ and/or $=O$. See the first part of paragraph **4)** of the first Office action. Applicants have not specifically responded to this rejection. Applicants' comments in the first paragraph of page 16 of the March 01, 2004 Remarks are directed to the preparation of compounds wherein R_4 is not hydrogen but do not address the preparation of the compounds wherein $-N(R_{11})(R_{12})$ and $=N(R_9)(R_{10})$ are replaced by $-OR_9$ and/or $=O$. Note that the

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compounds JF 22, JF 17, JF 30, JF 32, JF 36 and JF 37 all contain the $-N(R_{11})(R_{12})$ and $=N^+(R_9)(R_{10})$ groups.

7) Claims 20-25 and 44-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over each of **a)** Hallas (reference Y of form PTO-1449), Aaron et al (X) (reference X of form PTO-1449), Aaron et al [R] (J. Chem. Soc. (1963) pp. 2655-2662), Barker et al (J. Chem. Soc. [Section B: Physical Organic] (1969), vol. 9, pp 1068-1071), or Mueller et al (U.S. 4,320,940) taken in combination with each of **b)** Dorval et al (U.S. 5,561,045) or Bandman et al (U.S. 6,183,968) for the reasons stated in paragraph **15)** of the first Office action.

Applicants' arguments filed March 01, 2004 have been fully considered but they are not persuasive. Applicants have apparently failed to recognize that, unlike the compounds of claim 26, the compounds of claims 20-25 and 40-47 do not require the presence of at least **five** rings in the basic core structure. Thus, the fluorescent **three**-ring structures of instant claims 20-25 and 40-47 are described in references **a)** as set forth in paragraph **12)** of the first Office action. As stated in the first Office action, given the fact that a wide variety of fluorescent dyes are known to be useful as labels in immunoassays and nucleic acid hybridization assays (references **b)**, including "cationic dyes" as described by Dorval et al), it would be obvious to substitute the fluorescent dyes of reference **a)** as equivalent fluorescent labels in the immunoassays and nucleic acid hybridization assays of references **b)**, as claimed, with the expectation of obtaining similarly useful assays based on a fluorescence detection method.

8) Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH

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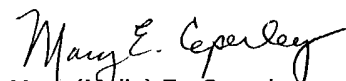
shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9) An inquiry of a general nature which is **not related to the prosecution on the merits** should be directed to Technology Center 1600 telephone number (571) 272-1600. The general fax number for the USPTO is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary (Molly) E. Ceperley whose telephone number is (571) 272-0813. The examiner can normally be reached from 8 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le, can be reached on (571) 272-0823.

May 27, 2004


Mary (Molly) E. Ceperley
Primary Examiner
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